UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/724,292	12/01/2003	Juan Armendariz Borunda	5585-036-999	4513

9629 7590 02/05/2007
MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/724,292	ARMENDARIZ BORUNDA ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22 and 24-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22 and 24-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12-29-06 has been entered.

Applicants' amendment and declaration under 37 CFR 1.131 filed on 12-29-06 have been entered. Claims 22 and 28-32 have been amended. Claims 22 and 24-32 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "the therapeutic proteins for the treatment of fibrotic disorders **is** selected from" in claim 22 is vague and renders the claim indefinite. The phrase "the therapeutic proteins" appears to mean more than one protein, however, the term "is" means only one protein. It is unclear how many therapeutic proteins are intended.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 22 and 24-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 22 and 24-32 are directed to a pharmaceutical composition comprising a therapeutically effective amount of unitary doses of viral particles of recombinant adenoviral vectors containing a therapeutic gene or DNA sequence under the control of a ubiquitous promoter, a tissue-specific promoter or a combination thereof, for the treatment of fibrotic disorders in organs and a pharmaceutically acceptable carrier, and a method of treating fibrotic disorders, such as hepatic fibrosis, pulmonary fibrosis, renal fibrosis, keloids, hypertrophic scars, or combination thereof, in a patient by delivering a recombinant adenoviral vector expressing therapeutic proteins via an administration route to an organ. Claim 25 specifies the administration route is intravenous. Claims 28-32 specify the therapeutic protein for the treatment of fibrotic disorders is MMP-8, MMP-1, truncated receptor for TGF-beta type II, wild type or modified uPA or combination thereof, and HGF, respectively.

The specification discloses that the rat models, including healthy rats, rats intoxicated with carbon tetrachloride (CCl4) and rats with ligation of the bile duct (LCB), receive infusion of Ad5gal vector by iliac vein shows that the main target organ of the infused adenoviral vector is

the liver. The spleen and the lung present a transduction grade lower than 1% and other organs, such as kidney, heart and brain, show no transduction at all (specification, pages 12-16).

The specification states "[t]he present invention relates to the creation of RECOMBINANT ADENOVIRAL vectors bearing exogenous genes that encodes for therapeutic proteins useful in the treatment of HEPATIC cirrhosis and generalized FIBROSIS, such as renal FIBROSIS, pulmonary FIBROSIS, HYPERTROPHIC scars and keloid of the skin, and/or in other target organs susceptible to suffer from it" and "the invention provides an effective way for the treatment of fibrosis through the employment of recombinant adenoviral vectors which are claimed here, as well as the process to prepare these vectors, the pharmaceutical composition that contains them, and their therapeutic uses in the treatment of several fibrosis" (specification, page 1, first and second paragraphs). The "pharmaceutical composition" implies therapeutic use of said composition. Thus, the claims read on gene therapy for the treatment of various fibrotic diseases or disorders in vivo.

The claims encompass treating various fibrotic diseases or disorders in a patient by delivering a recombinant adenoviral vector expressing a therapeutic protein under the control of a promoter to various target organs via various administration routes in vivo. The specification fails to provide adequate guidance and evidence for delivering a recombinant adenoviral vector expressing any therapeutic protein under the control of a promoter via various administration routes in vivo such that sufficient therapeutic protein can be obtained so as to provide therapeutic effects in target organs for treating any fibrotic disease or disorder in a patient.

The claims read on gene transfer and gene therapy in vivo. The nature of the invention being gene therapy, the state of the prior art was not well developed and was highly

unpredictable at the time of filing. While progress has been made in recent years for gene transfer *in vivo*, vector targeting to desired tissues *in vivo* continues to be unpredictable and inefficient as supported by numerous teachings available in the art. For example, Deonarain, M., 1998 (Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicates that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Verma et al., Sept. 1997 (Nature, Vol. 389, pages 239-242) reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Verma states that "The Achilles heel of gene therapy is gene delivery, and this is the aspect that we will concentrate on here. Thus far, the problem has been an inability to deliver genes efficiently and to obtain sustained expression...The use of viruses (viral vectors) is powerful technique, because many of them have evolved a specific machinery to deliver DNA to cells, However, humans have an immune system to fight off the virus, and our attempts to deliver genes in viral vectors have been confronted by these host responses." (e.g. p. 239, column 3). The adenoviral vector can induce both cell-killing "cellular" immune response and the antibody-producing "humoral" immune response from the host. The virally infected cells can be killed by cytotoxic T lymphocytes and the humoral response results in the generation of antibodies against adenoviral proteins. "There are considerable

immunological problems to be overcome before adenoviral vectors can be used to deliver genes and produce sustained expression" (e.g. p. 241, left and middle column).

Eck et al., 1996 (Goodman & Gilman's The Pharmacological Basis of Therapeutics, McGraw-Hill, New York, p. 77-101) states that the fate of the DNA vector itself (volume of distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, and the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced are all important factors for a successful gene therapy (e.g. bridging pages 81-82). In addition, Gorecki, 2001 (Expert Opin. Emerging Drugs, 6(2): 187-198) reports that "the choice of vectors and delivery routes depends on the nature of the target cells and the required levels and stability of expression" for gene therapy, and obstacles to gene therapy *in vivo* include "the development of effective clinical products" and "the low levels and stability of expression and immune responses to vectors and/or gene products" (e.g. abstract). Thus, administration route plays an important role in gene transfer efficiency.

Further, the administration route includes oral administration, intraperitoneal injection, topical administration, intravenous administration, intramuscular injection, and subcutaneous administration etc. As discussed above, the specification discloses that infusion of Ad5gal vector into rats by iliac vein shows that the main target organ of the infused adenoviral vector is the liver. Other organs, such as spleen, lung, kidney, heart and brain, show either very low transduction efficiency or no transduction at all. It appears that when an adenoviral vector is

administered via infusion or intravenous administration, most of the adenoviral vector reaches the liver but very little reaches other organs. The specification fails to provide adequate guidance and evidence for whether intravenous administration of an adenoviral vector to a patient could provide sufficient expression of a therapeutic protein in any organ other than the liver in said patient so as to provide therapeutic effect for treating various fibrotic disorders in different organs. The specification also fails to provide adequate guidance and evidence for whether various administration routes of an adenoviral vector to a patient could provide sufficient expression of a therapeutic protein in any organ, including the liver, in said patient so as to provide therapeutic effect for treating various fibrotic disorders in different organs. There is no evidence of record that shows administration of a recombinant adenoviral vector expressing a therapeutic protein under the control of a promoter or a combination of promoters into a patient via various administration routes can provide therapeutic effects for treating various fibrotic disorders or diseases in said patient. Therefore, one skilled in the art would not know how to use the recombinant adenoviral vector for treating various fibrotic diseases or disorders via various administration routes in vivo.

The claims also encompass using nucleotide sequences encoding various therapeutic proteins for treating various fibrotic diseases or disorders in a patient. However, different therapeutic proteins have different amino acid sequences and their biological functions would differ. The specification fails to provide adequate guidance and evidence for whether the claimed therapeutic protein or combination of therapeutic proteins would be able to treat various fibrotic diseases or disorders in different organs in vivo. It was known in the art that the amino acid sequence of a protein determines its structural and functional properties, and predictability

of which amino acids can be removed from a protein's sequence and still result in similar activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's structure from mere sequence data are limited. Rudinger, 1976 (Peptide Hormones, Edited by Parsons, University Park Press, Baltimore, p. 1-7), points out that "The significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study" (e.g. p. 6). Kaye et al., 1990 (Proc. Natl. Acad. Sci. USA, Vol. 87, pp. 6922-6926) teaches that "A single amino acid substitution results in a retinoblastoma protein defective in phosphorylation and oncoprotein binding" (e.g. Title). Davis, C. G., 1990 (The New Biologist, Vol. 2, No. 5, p. 410-419) reports that EGF repeats appears in an extraordinarily diverse group of molecules, including growth factors, transmembrane molecules, extracellular matrix proteins, and soluble secreted proteins, and it is often difficult to deduce what contribution the EGF repeat makes in a totally unrelated protein (e.g. p. 410, left column). It appears that EGF repeat can contribute to different biological functions in different amino acid contexts, i.e. different proteins.

Further, Skolnick et al., 2000 (Trends in Biotech, Vol. 18, p. 34-39) states "Sequence-based methods for function prediction are inadequate because of the multifunctional nature of proteins. However, just knowing the structure of the protein is also insufficient for prediction of multiple functional sites. Structural descriptors for protein functional sites are crucial for unlocking the secrets in both the sequence and structural-genomics projects" (e.g. abstract). Skolnick further states that "Knowing a protein's structure does not necessarily tell you its function" and "Because proteins can have similar folds but different functions, determining the

structure of a protein may or may not tell you something about its function" (e.g. p. 36, box 2). Therefore, biological function of a protein was unpredictable from mere amino acid sequence at the time of the invention and even same short stretch of amino acid sequence can show diverse biological functions while surrounded by different background amino acid sequences. There is no evidence of record that the claimed adenoviral vector expressing the recited therapeutic protein or combination of therapeutic proteins would be able to provide therapeutic effect in vivo so as to treat various fibrotic diseases or disorders in different organs. Therefore, one skilled in the art at the time of the invention would not know how to use the claimed adenoviral vector to treat various fibrotic diseases or disorders in vivo.

In view of the unpredictable nature of gene therapy in vivo, the limitation of using adenoviral vectors in gene delivery, and the unpredictable biological function of a protein from mere amino acid sequence, one skilled in the art at the time of the invention would not know how to use the recombinant adenoviral vector expressing any therapeutic protein for treating various fibrotic diseases or disorders via various administration routes in vivo. One of skilled in the art would require to identify and characterize the nucleotide sequence of the therapeutic protein, trial and error experimentation to determine the biological function of various therapeutic proteins, preparation of adenoviral vectors expressing various therapeutic proteins, administration of said viral vectors into a subject via various administration routes, trial and error experimentation to determine whether sufficient therapeutic protein is expressed at the target organ via various administration routes, and trial and error experimentation to determine whether the expressed therapeutic protein can provide therapeutic effect for treating various fibrotic diseases or disorders in vivo.

For the reasons discussed above, it would have required undue experimentation for one skilled in the art at the time of the invention to practice over the full scope of the invention claimed. This is particularly true given the nature of the invention, the state of the prior art, the breadth of the claims, the amount of experimentation necessary, the level of ordinary skill which is high, the working examples provided and scarcity of guidance in the specification, and the unpredictable nature of the art.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 22 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Li et al., August 1998 (Gene Therapy, Vol. 5, p. 1105-1113).

Claims 22 and 31 are directed to a pharmaceutical composition comprising a therapeutically effective amount of unitary doses, about 10^7 to about 10^{14}, of viral particles of recombinant adenoviral vectors containing a therapeutic gene or DNA sequence encoding the recited protein under the control of a ubiquitous promoter, a tissue-specific promoter or a combination thereof, for the treatment of fibrotic disorders in organs and a pharmaceutically

acceptable carrier. Claim 31 specifies the therapeutic protein is wild type or modified uPA of combination thereof.

Li teaches preparation of a recombinant adenovirus (AdmATF) encoding a secreted version of the amino-terminal fragment (ATF) of murine urokinase (uPA) under the control of CMV promoter (e.g. abstract, p. 1106, left column, second full paragraph). Li further teaches using 10^9 p.f.u. of AdmATF for intratumoral injection in mice (e.g. Figure 3). The secreted version of the amino-terminal fragment (ATF) of murine urokinase (uPA) is a modified uPA. CMV promoter is a ubiquitous promoter. 10^9 p.f.u. of adenovirus is in the range of about 10^7 to about 10^{14} of viral particles. The buffer solution containing the adenovirus is considered a pharmaceutically compatible carrier. Thus, claims 22 and 31 are anticipated by Li.

It should be noted that the intended use of the claimed recombinant adenoviral vector does not carry weight in the 102(b) rejection. The cited reference teaches every limitation of the claims.

7. Claims 22 and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Kay et al., 1999 (US Patent No. 5,980,886).

Claims 22 and 31 are directed to a pharmaceutical composition comprising a therapeutically effective amount of unitary doses, about 10^7 to about 10^{14}, of viral particles of recombinant adenoviral vectors containing a therapeutic gene or DNA sequence encoding the recited protein under the control of a ubiquitous promoter, a tissue-specific promoter or a combination thereof, for the treatment of fibrotic disorders in organs and a pharmaceutically

acceptable carrier. Claim 31 specifies the therapeutic protein is wild type or modified uPA of combination thereof.

Kay teaches construction of adenovirus expressing urokinase plasminogen activator (uPA) or modified uPA under the control of an inducible promoter or a constitutive promoter for transduction of hepatocytes and expression of uPA protein in said hepatocytes (e.g. abstract, column 6, lines 27-29, column 8, lines 8-9). Kay teaches preparation of AdRSV-uPA expressing human uPA under the control of RSV-LTR promoter and $0.5x10^{10}$ or $1x10^{10}$ pfu of the adenovirus were injected into the portal vein of mice (e.g. Example 1). Kay further teaches preparation of a recombinant adenovirus expressing modified uPA under the control of either RSV-LTR or PGK promoter and the recombinant adenovirus with PGK promoter was infused into the portal vein of mice (e.g. Example III, column 15, column 17, last paragraph). The buffer solution containing the adenovirus is considered a pharmaceutically compatible carrier. Thus, claims 22 and 31 are anticipated by Kay.

It should be noted that the intended use of the claimed recombinant adenoviral vector does not carry weight in the 102(e) rejection. The cited reference teaches every limitation of the claims.

Priority

8. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

It is noted that the foreign publication MEXICO 998515, filed on 9-17-99, was not published in English and no English translation for said foreign publication has been provided.

The foreign publication MEXICO 998515 can not be considered by examiner. Therefore, the following 102(b) rejection that appears in previous Official action is maintained.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 22 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Hattori et al., January 1999 (Human Gene Therapy, Vol. 10, no. 2, pp. 215-222).

Claims 22 and 31 are directed to a pharmaceutical composition comprising a therapeutically effective amount of unitary doses, about 10^7 to about 10^{14}, of viral particles of recombinant adenoviral vectors containing a therapeutic gene or DNA sequence encoding the recited protein under the control of a ubiquitous promoter, a tissue-specific promoter or a combination thereof, for the treatment of fibrotic disorders in organs and a pharmaceutically acceptable carrier. Claim 31 specifies the therapeutic protein is wild type or modified uPA of combination thereof.

Hattori teaches generation of recombinant adenoviruses containing human and mouse urokinase-type plasminogen activator (uPA) cDNA under the control of CMV promoter. A single intratracheal instillation of these uPA-containing adenoviruses into mouse lungs resulted in increased plasminogen activator activity in bronchoalveolar lavage fluid and the A549 cells infected with the adenoviruses can lyse plasma-derived fibrin-rich matrices in vitro (e.g. abstract,

p. 216, left column). Hattori teaches a single intratracheal instillation of 2.5 x 10^8 PFU of virus into mice results in greater PA activity as compared to control (e.g. p. 218, left column). The uPA gene encodes a therapeutic protein for treating the fibrotic disorders in organs. The dose of 2.5 x 10^8 PFU of the adenovirus falls within the range of 10^7-10^{14} viral particles. Thus, claims 22 and 23 are anticipated by Hattori.

It should be noted that the intended use of the claimed composition does not carry weight in the 35 U.S.C. 102(b) rejection.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of

the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER